

Amendments to the Specification:

Please amend the Title of the Invention as follows:

METHOD OF DETECTING METASTASIZING CANCER CELLS  
ORIGINATING IN STOMACH CANCER

In paragraph [0006] please amend to read as follows:

[0006] To improve the prognosis for gastric cancer, the inventors have developed a prevention for recurrence of gastric cancer with positive serosal invasion by intraperitoneal administration of mitomycin C adsorbed on activated charcoal particles (MMC-CH). However, intraperitoneal cancer chemotherapy such as MMC-CH is associated with side effects such as thrombocytopenia and ileus. Therefore, it is necessary to confirm the possibility of metastasis of gastric cancer cells to ~~the peritoneum~~ the peritoneal cavity and rapidly determine whether the peritoneal cancer chemotherapy should be applied or not.

In paragraph [0007] please amend to read as follows:

[0007] For the diagnosis of cancer of the digestive system, CEA (carcinoembryonic antigen) is generally used as a marker, and the use of rapid quantitative RT-PCR analysis using this as an indicator for detection of peritoneal free cancer cells has been domestically proposed by Aichi Cancer Center, etc. However, since this marker is weakly expressed in normal epidermal cells and mesothelial cells, there are many cases of false-positive determination, thus presenting a problem in detection of cancer cells in ~~the peritoneum~~ the peritoneal cavity.

In paragraph [0009] please amend to read as follows:

[0009] In order to find a highly specific marker to rapidly determine whether or not gastric cancer is metastatic to ~~the peritoneum~~ the peritoneal cavity, the inventors analyzed expression profiles of about 21,000 genes in cell lines derived from peritoneally disseminated gastric cancer,

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SNU-5, SNU-16, SNU-719, KATO-III and GT3TKB cells, with the use of a cDNA microarray. As the control, a cell line derived from primary gastric cancer focus, SNU-1, was used. About 20 genes that showed highly specific expressions in the cells derived from peritoneally disseminated gastric cancer but showed no expressions or extremely weak expressions in the cells derived from primary focus of gastric cancer were identified.

In paragraph [0010] please amend to read as follows:

[0010] Further, it was studied whether or not the above 20 genes specific for the cells derived from peritoneally disseminated gastric cancer could be applied to diagnosis of the presence of minute cancer cells in ~~the peritoneum~~ the peritoneal cavity and rapid intraoperative diagnosis thereof by combining the change in gene expression and an analysis by Northern blotting or RT-PCR. The results identified genes having sensitivity and specificity equal to or higher than CEA.

In paragraph [0019] please amend to read as follows:

[0019] The biological sample of a subject is not particularly limited as long as it is derived from ~~the peritoneum~~ the peritoneal cavity, and specifically exemplified by celiac tissues such as peritoneum of the subject, ascites fluid, cells contained in intraoperative peritoneal lavage, and peritoneal lavage fluid (lavage fluid recovered after subjecting to peritoneal lavage). Particularly, ascites fluid, cells in intraoperative peritoneal lavage, and peritoneal lavage fluid are preferred because these are easy to obtain. It should be noted that cancer cells that originated from primary gastric cancer cells and metastasized to ~~the peritoneum~~ the peritoneal cavity are collectively called "metastatic cancer cells" in the present specification. The metastatic cancer cells include, for example, peritoneal free cancer cells, cancer cells in ascites fluid of gastric cancer, peritoneal dissemination, and the like. Subject means patient, particularly cancer patient, and preferably patient suspected of peritoneal metastasis of gastric cancer.

In paragraph [0036] please amend to read as follows:

[0036] According to the present invention, aldehyde dehydrogenase, dopa decarboxylase, or both of them can be used as markers for detection of peritoneal free cancer cells that can be applied to diagnosis of the presence of minute cancer cells in ~~the peritoneum~~ the peritoneal cavity and rapid intraoperative diagnosis. Aldehyde dehydrogenase or dopa decarboxylase is not expressed in normal epithelial cells and mesothelial cells in contrast with CEA that has been conventionally used as a detection marker, and therefore, peritoneal free cancer can be detected with high specificity and high accuracy by detecting expression of aldehyde dehydrogenase or dopa

decarboxylase. The presence or absence of peritoneal dissemination of a subject is detected with high accuracy by examining the presence or absence of expression of aldehyde dehydrogenase or dopa decarboxylase, thereby allowing it to be used as one of the guidelines for whether or not subsequent intraperitoneal cancer chemotherapy is performed.

In paragraph [0052] please amend to read as follows:

[0052] From the results in examples 1 and 2, aldehyde dehydrogenase and dopa decarboxylase were not expressed in the primary gastric cancer cells or their expression levels were extremely low, while these were upregulated in the cells derived from peritoneally disseminated gastric cancer, and therefore, it was considered that an examination of these expressions might be used for the diagnosis of the presence of minute cancer cells in ~~the peritoneum~~ the peritoneal cavity. In order to confirm whether or not the expression of these genes could be applied to the diagnosis of the presence of minute cancer cells in ~~the peritoneum~~ the peritoneal cavity, the expression of aldehyde dehydrogenase and dopa decarboxylase was determined by RT-PCR in 18 patients with serosal invasion-positive gastric cancer uncertain about actual peritoneal metastasis using 12 patients with carcinomatous peritonitis of gastric cancer and 21 patients with no cancer as positive and negative controls, respectively, among cases of gastric cancer surgery performed at the Division of Digestive Surgery, Kyoto Prefectural University of Medicine.